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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/857,691 | 09/05/2001 | Angus George Dalgleish | 37945-0018 | 6462 |

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HELLER EHRMAN WHITE & MCAULIFFE LLP
1666 K STREET,NW
SUITE 300
WASHINGTON, DC 20006

| EXAMINER | |
|---|---|
| DAVIS, MINH TAM B | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 03/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/857,691 | DALGLEISH ET AL. | |
| | Examiner | Art Unit | |
| | MINH-TAM DAVIS | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,11,12,23 and 24* is/are pending in the application.

4a) Of the above claim(s) *23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant adds new claims 23, 24.

Since applicant has elected Group II, a composition comprising a combination of a single human non-cancerous prostate cell line, PNT2, a cancerous prostate cell line LNCaP and a primary prostate cell line, NIH-1542, for action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the embodiments of claims 23- 24 directed to a composition comprising at least two or all three non-cancerous human prostate cell lines have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 1.142(b) and M.P.E.P. 821.03. Newly submitted claims 23-24 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

They comprise three different cell lines with different characteristics or properties.

Accordingly, claims 1, 11, 12 are being examined, wherein claims 1, 11, 12 are examined only to the extent of a combination of one non-cancerous prostate cell line, PNT2, one cancerous prostate cell lines LNCaP and one primary prostate cell line, NIH-1542.

This application contains claims drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of

nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The following are the remaining rejections.

**REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER**

Claims 1, 11-12 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of "at least" one human prostate cell line is non-cancerous claimed in Claim 1 has no clear support in the specification and the claims as originally filed. A review of the specification discloses support for a vaccine which may be based on one or a combination of different immortalized normal cells derived from the prostate (p.4, paragraph before last). **The subject matter claimed in claim 1 broadens the scope of the invention as originally disclosed in the specification.**

**REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT**

Rejection under 35 USC 112, first paragraph of claims 1, 11-12 pertaining to lack of enablement for an allogeneic immunotherapeutic agent for the treatment of prostate cancer remains for reasons already of record in paper No.13.

Applicant submits a Declaration by Dr. Anthony Walker. Applicant asserts in the Declaration that Applicant possesses data from:

1) clinical trial of human prostate cancer, using LNCaP, a metastatic human prostate cell line, NIH-1542, a primary human prostate cell line, and PNT2, a normal human prostate cell line,

2) treating mouse melanoma with mouse non-cancerous cell line,

3) treating a mouse model of prostate cancer, using a mouse normal prostate cell line and a tumorigenic mouse prostate cell line RM9 and

4) treating a mouse renal cancer, using a mouse non-cancerous renal cell line, and a mouse tumorigenic renal cell line RenCa.

Applicant asserts that thus all the data point to the general principle that the use of an immortalized normal cell line is useful invention that can be applied across many different tumors.

In the Declaration, Applicant asserts that the references by Wu et al, Sartor et al, D'Amico et al, Pound et al, Roberts et al and Vollmer et al, all teach that an increased PSA level is associated with prostate cancer, and that the reverse principle should be applied, i.e. a decreased PSA level should indicates that prostate cancer is effectively treated.

Applicant asserts that the instant immunotherapeutic agent works through stimulation of the immune system.

Applicant further asserts that the references cited on page 4 of the specification teach the use of cell-based cancer vaccines based on prostate cell lines.

The submission of the Declaration by Dr. Anthony Walker, and the recitation of Wu et al, Sartor et al, D'Amico et al, Pound et al, Roberts et al and Vollmer et al are acknowledged and entered.

Applicant's arguments set forth in paper of 12/01/03 have been considered but are not deemed to be persuasive for the following reasons:

Contrary to Applicant's assertion, no data have been submitted that point to the general principle that the use of an immortalized normal cell line is useful invention that can be applied across many different tumors. Further, it is noted that there are no data showing that human prostate cancer is effectively treated by human prostate cell lines in the Declaration by Dr. Anthony Walker, nor in the art and the specification. It is not clear on what basis that Applicant claims that a combination of three human prostate cell lines, PNT2, LnCaP, and NIH-1542, one of said cell lines is a non-cancerous prostate cell line, would be effective in treating prostate cancer, in view of the overwhelming teaching in the art that cancer treatment is unpredictable, as taught by Gura et al, Jain et al, Curti et al, and Hartwell et al (all of record). Further, even an immune response is elicited in prostate cancer patients, such as T cell responses, as asserted by Applicant in the response, one still cannot predict that said immune response is effective for treating cancer. For example, Boon (Adv Can Res, 1992, 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization and several lines of evidence suggest that large tumor

burdens can tolerize or at least depress the capability to respond against the tumor (p. 206, para 2). In addition, Boon teaches even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells (p.178, paragraph before last paragraph).

Further, although an increased PSA level is known to be associated with prostate cancer, the reverse could not necessarily be applied, in view that the level of PSA could be reduced by the induction of antibodies produced by the administered prostate cancer cell lines that produce PSA, or having PSA on their cell surface, and thus one cannot assess whether a reduction in PSA level is due an induced production of anti-PSA antibodies, or a reduction in the growth of prostate cancer cells.

Moreover, concerning the prior art references cited on page 4 in the specification, none of said references teach treating prostate cancer, using prostate cancer cell lines. The immunogenicity of cancer cell lines other than prostate cancer cell lines is not necessarily the same as that of prostate cancer cell lines, and this could have an important influence on the effectiveness of treatment of prostate cancer. For example, in one the references cited on page 4 of the specification, it was shown that irradiated melanoma B16 cells alone fail to induce systemic protection, and that only B16 cells transduced with one of the most potent cytokine, GM-CSF, are effective (WO 93/06867, p.38, second paragraph). In other words, the main anti-tumor activity is due to GM-CSF. The reference went on teaching that the generation of systemic immunity in non- or

poorly immunogenic tumors may thus require qualitatively different mechanisms than those responsible for inducing this immunity in more immunogenic tumors.

Thus one cannot extrapolate the treatment of other cancers, such as melanoma, to treatment of prostate cancer, because the type and the degree of antigenic stimulus by other cancers such as melanoma cells relevant to cancer cell growth are not necessarily similar to those of prostate cells, and because different diseases have different etiology and different responses to therapeutic agents.

Concerning the mouse model for prostate cancer, in the absence of objective evidence, one cannot assess the claim that non-cancerous prostate cell lines could be effectively used for treating mouse prostate cancer. Further, Applicant has not shown that the mouse model recently established by Applicant is representative of human prostate cancer, because it is well known in the art that human prostate cancer is a very slow type of cancer, and it is questionable that the mouse prostate cancer has the same characteristics or properties of human prostate cancer.

In view of the above, one cannot predict that the claimed human prostate cell lines would be useful for treating human prostate cancer.

**REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE**

1. Rejection under 35 USC 112, first paragraph of claims 1, 11-12 pertaining to lack of enablement for an allogeneic immunotherapeutic agent for the

treatment of prostate cancer comprising at least one of "any" non-cancerous human prostate cell lines remains for reasons already of record in paper No.13.

Applicant asserts that the teaching of the instant specification can apply to many combinations of cells, as shown in the Walker Declaration.

Applicant's arguments set forth in paper of 12/01/03 have been considered but are not deemed to be persuasive for the following reasons:

The Walker Declaration has not shown that human prostate cancer could be treated by any combination of any human prostate cell lines, *supra*.

The scope of the claims are drawn to any human non-cancerous prostate cell lines, wherein the characteristics and properties of said cell lines are not known, such as the degree of their immunogenicity, which would have a significant influence on the immune response and immunotherapy of human prostate cancer. Further, since it is difficult to establish non-cancerous prostate human cell lines, and there is only a handful of human prostate cell lines derived from normal tissues presently established, as taught by Berthon et al, of record, the claimed any human non-cancerous prostate cell lines are yet to be established.

2. Rejection under 35 USC 112, first paragraph of claims 1, 11-12 pertaining to lack of enablement for an allogeneic immunotherapeutic agent for the treatment of prostate cancer comprising "alive" cancerous human prostate cell lines remains for reasons already of record in paper No.13.

Applicant argues that because the claimed vaccine cells are mismatched to the patient being treated, and thus they will be rejected and will not cause cancer.

Applicant's arguments set forth in paper of 12/01/03 have been considered but are not deemed to be persuasive for the following reasons:

Applicant argues limitation not in the claims. Further, the specification does not disclose that the patients being treated have a mismatched LNCaP, a tumorigenic cell line, and thus one would expect that said patient will develop, in addition, metastatic prostate cancer, in view of the teaching of Wu et al, and Triest et al, of record.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, YVONNE EYLER can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

March 04, 2004

SUSAN UNGAR, PH.D
PRIMARY EXAMINER